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Research Article

Medical Marijuana: A Comprehensive Review on Therapeutic Use, Legal Bindings and Regulatory Perspectives

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ABSTRACT

For thousands of years, cannabis has been used medicinally. A recent rise in its use has sparked important academic and legal debates. The medical advantages, modes of action, dangers, and legal ramifications of cannabis use are all examined in this paper. Numerous ailments, such as neurodegenerative diseases, psychiatric disorders, epilepsy, glaucoma, multiple sclerosis, chronic pain, nausea brought on by chemotherapy have been effectively treated with cannabis-based therapies. Cannabis usage has both immediate and long-term side effects, such as dependency, cognitive impairment, cardiovascular problems, and negative impacts on mental health, despite its therapeutic potential. Concerns about safety and quality control are raised by the variation in cannabis products, dosage, and regulation. Prescribing unstandardised cannabis-based medicines also presents ethical challenges. Although there are still a lot of unanswered questions, legalisation patterns in different areas continue to influence the availability and acceptance of medicinal cannabis. Further research is needed to confirm its effectiveness, improve dosage plans, and reduce any possible health hazards. This review offers a thorough summary of the available data, emphasising the potential and difficulties related to medical cannabis.

Keywords: Cannabis, Marijuana, Cannabinoids, Medical Cannabis, Regulation and Legalization

INTRODUCTION

Despite cannabis being utilised for medical purposes for millennia, its recent resurgence has ignited significant scholarly interest and legal debates. Advocates of medicinal cannabis support its usage for a variety of ailments, most notably pain relief and multiple sclerosis. Recent results from population-based surveys in the US and Canada show that cannabis usage is more prevalent and frequent among those with mental health issues [1]. The results of recent population-based surveys conducted in the US and Canada support the notion that cannabis usage is more common and frequent among those with mental health issues. Delta-9-tetrahydrocannabinol, cannabidiol, tetrahydro-cannabivarin, endocannabinoids, cannabis, and more than 60 other cannabinoid compounds—some of which have opposing effects—are among the more than 400 chemical entities found in the complex plant known as cannabis. Cannabis is the third most popular drug after alcohol and tobacco, and it has been used recreationally for thousands of years. Cannabis was originally used medicinally approximately 400 AD. Although there have been reports of cannabis use in India for at least a few thousand years, it wasn't until the 1800s that cannabis cultivation and use spread quickly both domestically and internationally. This was because nonpsychoactive hemp became a valuable cash crop, and the British

rulers of India ordered the mass cultivation of cannabis, which in turn led to an increase in cannabis use rates. With the passage of the Compassionate Use Act in 1996, California became the first state to allow legal access to and use of botanical cannabis for medical purposes under physician supervision [2,3].

2. Mechanism of action of cannabinoids

Cannabinoids work by interacting with the body's endocannabinoid system (ECS), a sophisticated cell-signalling system that controls immune response, mood, pain, appetite, and memory.

2.1 The Endocannabinoid System (ECS)

The principal mechanism that cannabinoids have therapeutic benefits is through the endocannabinoid system (ECS), a ubiquitous neuromodulatory system that regulates immune responses, appetite, mood, memory, pain perception, and synaptic transmission. The ECS is composed of endogenous ligands (endocannabinoids), cannabinoid receptors (CB1 and CB2), and the enzymes that produce and break them down. While cannabidiol (CBD) is a non-intoxicating component with distinct pharmacological properties, delta-9-tetrahydrocannabinol (THC) is the primary psychoactive phytocannabinoid derived from Cannabis sativa [4].

Cannabinoids mainly function by activating G-protein-coupled receptors (GPCRs), which are cannabinoid receptors. CB1 receptors are mainly found in the central nervous system, specifically in the cerebral cortex, hippocampus, basal ganglia, cerebellum, and spinal cord, whereas CB2 receptors are mostly found in immune cells and peripheral tissues. When a cannabinoid, like THC, binds to CB1 or CB2 receptors, the inhibitory Gi/o protein is triggered. This activation results in the alpha subunit of the G-protein exchanging GDP for GTP, which separates the alpha and beta-gamma subunits and modifies intracellular signalling pathways [5].

Cannabinoids also have a major effect on ion channel activity. The amount of calcium that enters presynaptic neurones is reduced when voltage-gated calcium channels are blocked by the beta-gamma subunits of the activated G-protein. Since vesicular neurotransmitter release requires calcium entry, this inhibition lessens the release of excitatory and inhibitory neurotransmitters such glutamate, GABA, dopamine, norepinephrine, acetylcholine, and serotonin. By activating inwardly rectifying potassium channels, cannabinoids simultaneously increase potassium outflow and promote membrane hyperpolarisation. This reduces neuronal excitability, which further impedes synaptic transmission. Thus, cannabinoids primarily act as presynaptic inhibitors of neurotransmitter release [6].

One unique feature of the endocannabinoid system is retrograde signalling. When required, membrane phospholipids in the postsynaptic neurone are converted into endocannabinoids such anandamide and 2-arachidonoylglycerol. After being released, they diffuse backward across the synaptic cleft to engage presynaptic CB1 receptors. This retrograde mechanism establishes a feedback loop that regulates neuronal excitability and synaptic plasticity by stopping further neurotransmitter release from the presynaptic neurone [6].

THC mostly acts as a partial agonist at CB1 and CB2 receptors. Its stimulation of CB1 receptors in the brain, particularly in the mesolimbic dopamine pathway, is the main source of its psychoactive effects. By indirectly increasing dopamine release, it produces bliss. Activation of CB1 receptors in the hypothalamus promotes hunger, whereas activity in the brainstem produces antiemetic effects. Analgesia is produced by modulating both the spinal and supraspinal pain pathways. However, CBD has a limited affinity for CB1 and CB2 receptors and does not have a significant psychotropic effect. Instead, it acts as a negative allosteric modulator of CB1 receptors and inhibits the enzyme that breaks down anandamide, fatty acid amide hydrolase (FAAH), to raise endogenous cannabinoid levels. Furthermore, CBD interacts with non-cannabinoid targets like 5-HT1A serotonin receptors, which have anxiolytic effects, and TRPV1 receptors, which contribute to analgesic and anti-inflammatory effects. Through these several routes, CBD possesses neuroprotective, anxiolytic, and anticonvulsant qualities [7].

To sum up, cannabinoids mainly function by activating CB1 and CB2 Gi/o-coupled receptors, which suppresses the release of neurotransmitters, inhibits adenylyl cyclase, lowers cAMP, and regulates calcium and potassium channels. Retrograde synaptic transmission and further modulation of intracellular signalling pathways are responsible for their wide spectrum of central and peripheral pharmacological actions. Figure 1 demonstrates mechanism of activation of cannabinoids.

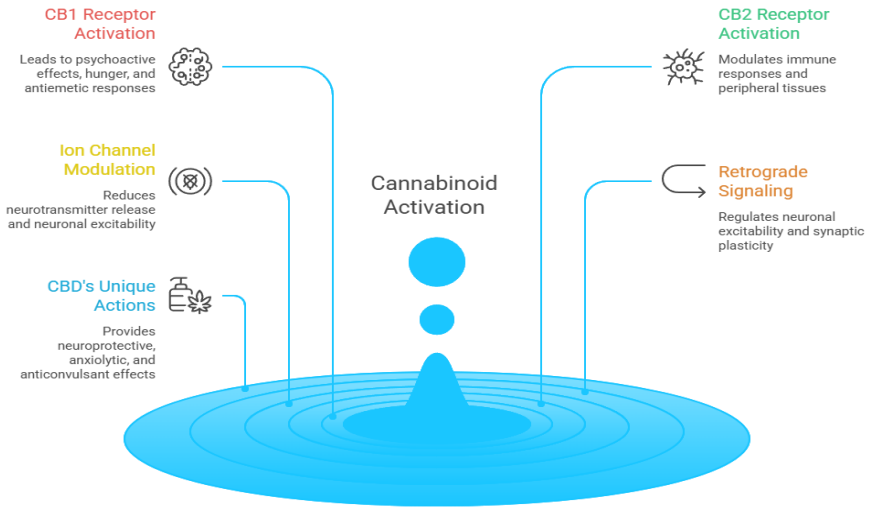

Figure 1. Mechanism of Action of Cannabinoids

3. Medical Uses of Cannabis

Cannabinoid medications and cannabis-based products are used professionally to treat nausea/vomiting, appetite loss/cachexia, spasticity in multiple sclerosis, chronic/neuropathic pain, and some epilepsies. They either target CB1/CB2 (mostly via THC) or operate via non-CB pathways (most notably CBD). Each chemical has a different regulatory status and receptor specificity [8]. Table 1 summarized the medical uses of cannabis and its structural analogues.

Table 1. Therapeutic Uses of Cannabinoids

Sr. No.	Drug or cannabis treatment	Therapeutic action	Medical Application	References
1	Dronabinol (synthetic THC)	Reduces nausea and vomiting	Chemotherapy-induced nausea and vomiting	[9,10]
		Regulates bowel movements and , decreases diarrhoea, Improves appetite	Irritable Bowel Syndrome	
		Neuroprotection	Alzheimer's Disease	
		Appetite stimulation	Cancer/ HIV associated anorexia	
2	Nabilone (synthetic cannabinoid)	Reduces nausea and vomiting	Chemotherapy-induced nausea and vomiting	[11, 12]
		Neuroprotection	Huntington's disease	
		Dyskinesia relief	Parkinson's disease	
3	Nabiximols (Sativex, THC:CBD ≈1:1)	Reduces spasticity and relief of neuropathic/chronic pain symptoms in some settings	Multiple sclerosis Spinal Cord Injury	[13]
4	Epidiolex / purified cannabidiol (CBD)	Reduces seizure	Drug-resistant epilepsies and seizure disorders	[14]
5	Cannabis flower, THC-dominant preparations	Anti-inflammatory action	Chronic pain	[14, 15]
		Reduces nausea and vomiting	Chemotherapy-induced nausea and vomiting	
		Reduces chronic pain	Peripheral neuropathy	
6	Cannabidiol	Reduces eye pressure	Glaucoma	[16]

		Reduces anxiety, depression, stress,	Psychiatric disorders	

4. Risks and Side Effects of Cannabis

Cannabis side effects can range from minor short-term effects like exhilaration, lightheadedness, and dry mouth to more severe long-term repercussions including dependence, respiratory issues, mental health issues, and cognitive impairment. The dosage, mode of administration, length of use, and individual sensitivity all affect how severe these effects are. [17, 18] The side effect of cannabis on body system is summarized in the Figure 2.

Figure 2. Side Effects of Cannabis

5. Quality Concerns of Cannabis

Medical cannabis quality is threatened by pesticide residues, heavy metals, and microbial contamination, while cannabinoid content and chemotypes are inconsistently measured and labelled. Fragmented regulation and variable testing/sampling create gaps in safety and standardization. The primary safety threats for medical cannabis are chemical and biological contaminants that can reach patients during cultivation, processing, or distribution; these include pesticides, heavy metals, and microbes. Evidence documents widespread pesticide residues in some markets, frequent detection of fungi and moulds on products, and recognition of elemental contaminants as important quality attributes for public-health standards [19].

6. Cannabinoid Standardization

Variability in cannabinoid content, uneven distribution across plant material, and inconsistent labeling undermine reproducible medical dosing and comparability across products. Expert and clinical recommendations emphasize the need for defined chemotype categories, validated quantitative assays, and routine titration or standardization for medical formulations [20].

6.1. Chemotype Classification

A USP expert panel recommends categorizing cannabis into THC-dominant, THC/CBD intermediate, and CBD-dominant chemotypes and using chromatographic identity and quantitative tests to define these categories.

6.2. Analytical Requirements

Quantitative determination of critical constituents (e.g., THC, CBD) and validated sampling procedures are necessary because cannabis is a heterogeneous matrix with uneven constituent distribution [21].

6.3. Pharmaceutical Preparations

For oral medical formulations, standardized titration and stabilized preparations (for example, oil-in-water emulsions with validated stability) are used to provide known doses and improve therapy uniformity.

6.4. Clinical Implication

Clinicians should prefer products with independent concentration testing and clear labelling to support dose titration and reduce variability in patient exposure.

7. Regulatory Challenges

Gaps in regulation, variable testing standards, and inconsistent enforcement create persistent risks for medical cannabis quality and patient safety. Multiple organizations have called for harmonized public-quality specifications, but implementation and surveillance remain inconsistent across jurisdictions [22].

7.1. Regulatory Variability

Products sold in regulated programs are held to higher standards (testing, decontamination, concentration limits), yet many markets lack consistent nationwide or international requirements for acceptance criteria and sampling methods [22].

7.2. Testing and Sampling Hurdles

Defining representative sampling, acceptance limits for pesticides, microbes, mycotoxins, and elemental contaminants, and standardized analytical procedures are central challenges identified by pharmacopeial experts

7.3. Evidence Gaps and Enforcement

Published surveys and case series reveal substantial contamination in some legal markets and underscore inconsistent mitigation across producers and dispensaries

7.4. Practical Consequence

Until harmonized standards, validated testing workflows, and transparent labeling are widely adopted, clinicians and patients face uncertainty about safety and dose reproducibility

8. Ethical And Legal Considerations Of Medical Cannabis

Medical cannabis raises standard clinical ethics issues — especially respect for patient autonomy and careful harm–benefit assessment — while regulation varies widely between federal and subnational systems. Legal risks exist for both patients and clinicians where laws or institutional policies conflict [23].

8.1. Medical Ethics

Medical ethics frame whether and how clinicians recommend cannabis; clinicians must balance patient choices with safety and social consequences. Key ethical duties invoked in the literature include respect for autonomy, assessment of risks and benefits, non-maleficence, and considerations of justice and stigma.

8.2. Autonomy

Clinicians should respect patients' informed choices and preserve a bona-fide doctor-patient relationship when considering cannabis therapy, including documenting rationale and informed consent practices.

8.3. Non-Maleficence And Beneficence

Physicians are advised to assess the risk–benefit ratio for each indication and avoid causing harm through unsafe prescribing or inadequate monitoring.

8.4. Justice And Social Effects

Prescribing policies must consider fairness of access, risks of stigmatization, diversion, and wider social harms that legalization or medicalization can produce.

8.5. Practical Safeguards

Recommendations include clinician education, formal registration or credentialing for prescribers, and clear eligibility criteria to align clinical ethics with regulatory expectations [24].

9. Regulatory Status

Legal frameworks for medical cannabis differ across countries and within federations, producing tensions between national and subnational rules. The literature highlights explicit conflicts where federal drug controls conflict with state or provincial medical programs and where national rescheduling or legalization alters clinical practice.

9.1. Federal Classification And Conflict

In settings where cannabis remains a federally controlled Schedule I substance, federal law can conflict with state medical laws [24].

9.2. State And Local Variation

Subnational legalization or medical programs can permit patient access even when federal law prohibits distribution, producing operational and legal dilemmas for clinicians and public systems

9.3. National Policy Differences

Some countries have moved to legalize or reschedule cannabis (affecting clinical availability and regulatory oversight), while others permit narrow medical use but impose strict prescribing constraints in practice

9.4. Institutional Rules

Federal systems may impose additional institutional restrictions (for example on federal health systems or benefit programs) that limit clinician behavior regardless of local laws [25].

10. Legal Risks Patients Of Medical Cannabis

Patients face variable legal and practical risks that depend on jurisdictional rules, institutional policies, and enforcement priorities. Reported concerns include criminal exposure in some settings, restricted access despite legal frameworks, and social or legal consequences from informal use.

10.1. Criminalization And Access Gaps

Even where medical programs exist, patients may still encounter criminalization, tight prescribing controls, or limited practical access that pushes some to self-medicate or seek nonregulated sources [26].

10.2. Stigma And Diversion Concerns

Legalization for medical use can still produce stigmatization and risks of diversion that affect patients socially and legally, especially in settings with weak regulatory controls.

10.3 Conflict With Federal Programs

Patients subject to federal systems (for example veterans using federally governed health services) may be eligible under state law yet face restrictions within federal programs or loss of benefits or services [26].

11. Legal Risks Providers Of Medical Cannabis

Providers must navigate ethical duties and regulatory exposure where federal, institutional, and local rules differ; the literature documents concrete professional risks and recommended mitigations. Clinicians may face licensing, employment, or prescribing consequences if they act inconsistently with controlling laws or institutional policies.

11.1. Regulatory And Professional Risk

Providers who recommend or facilitate access to cannabis can face regulatory scrutiny or loss of prescribing privileges where federal enforcement or professional rules conflict with local medical programs [27].

11.2. Institutional Constraints

Clinicians working in federally governed or institutionally regulated systems may be prohibited from involvement even when state law permits medical use, creating ethical and legal dilemmas in patient care.

11.3. Risk Mitigation Strategies

Suggested protections include following documented clinical criteria, obtaining informed consent, participating in prescriber education and registration programs, and adhering to institutional policies to reduce legal exposure.

11.4. Ethical Permissibility but Not Obligation

In some clinical contexts the literature concludes recommending medical cannabis is ethically permissible but not obligatory, giving clinicians professional discretion bounded by law and evidence [27].

CONCLUSION

Despite significant obstacles, cannabinoid research will continue to progress. There are several research gaps on the efficacy of cannabidiol or cannabidiol-enriched cannabis in the treatment of various illnesses. A pain condition that seems to have some potential evidence supporting the usage of medical cannabis is cancer-related pain. Even though studies have investigated the use of cannabis to treat cancer-related pain, the results only support a grade D recommendation. Another type of pain is neuropathic pain, which has been examined in prospective trials, although cannabis treatment for this indication is recommended with a grade C due to a lack of high-quality data.

There is currently insufficient information on the safety and effectiveness of using medical cannabis to treat chronic non-malignant pain disorders. To support ongoing research and gather information on the medical use of cannabis through extensive randomised controlled trials, transformational policy reform is required. Theoretically, these policy changes

will result in enhanced transparency, state and federal regulatory congruences, and consideration of stakeholder concerns to effectively adjust to growing public acceptance of medical cannabis and patient use of it.

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14. Conflict of Interest
Authors declare no conflict of interest

15. Ethical Approval
Not required

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